REC'D 10 MAY 2006
WIPO PCT

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:
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PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Applicant's or agent's file reference 514712001940	Date of mailing (*day/month/year*) 08 MAY 2006 **FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date (*day/month/year*)	Priority date (*day/month/year*)
PCT/US04/43435	23 December 2004 (23.12.2004)	23 December 2003 (23.12.2003)

International Patent Classification (IPC) or both national classification and IPC

IPC: **G01N 33/53**(2006.01);**C07K 16/28**(2006.01)
USPC: 424/85,88;435/7.1;530/388.22,387

Applicant

RINAT NEUROSCIENCE CORP.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I — Basis of the opinion
- ☐ Box No. II — Priority
- ☐ Box No. III — Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV — Lack of unity of invention
- ☒ Box No. V — Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI — Certain documents cited
- ☐ Box No. VII — Certain defects in the international application
- ☐ Box No. VIII — Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(*b*) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/ US	Date of completion of this opinion	Authorized officer
Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (571) 273-3201	22 February 2006 (22.02.2006)	Parthosh K. Tungaturthy Telephone No. (571) 272-8789

Form PCT/ISA/237 (cover sheet) (April 2005)

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US04/43435

Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of:

☒ the international application in the language in which it was filed

☐ a translation of the international application into _____, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

☒ a sequence listing

☐ table(s) related to the sequence listing

b. format of material

☒ on paper

☒ in electronic form

c. time of filing/furnishing

☒ contained in the international application as filed.

☒ filed together with the international application in electronic form.

☐ furnished subsequently to this Authority for the purposes of search.

3. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US04/43435

Box No. V Reasoned statement under Rule 43 *bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims NONE	YES
	Claims 1-25	NO
Inventive step (IS)	Claims NONE	YES
	Claims 1-25	NO
Industrial applicability (IA)	Claims 1-25	YES
	Claims NONE	NO

2. Citations and explanations:

Claims 1-25 lack an inventive step under PCT Article 33(3) as being obvious over Shelton et al (PGPUB 2005/0089521A1; Filed December 23, 2003, Claims priority to December 23rd, 2003) in view of Segal et al (U.S. Patent 4,676,980; Issue Date: June 30th, 1987), and further in view of Devaux et al (Filed October 30th, 2003).

The claims are summarized as an agonist anti-trkC antibody comprising a heavy chain variable region comprising CDRs 1-3 of SEQ ID NO:4-5 ; and a light chain variable region comprising a CDRs 1-3 of SEQ ID NO:7-9, in addition to interchanging the amino acid residues within the CDR regions, The claims further recite nucleic acid encoding an agonist anti-trkC antibody, a vector, a host cell, a pharmaceutical composition and a kit. The claims further recite a method of making an agonist anti-trkC antibody, said method comprising expressing a polynucleotide encoding the agonist anti-trkC antibody, in addition to a polypeptide that binds to trkC comprising the said CDRs and the said changes within the CDR.

Shelton teaches an agonist anti-trkC antibody comprising a heavy chain variable region comprising a CDR1-3 of SEQ ID NO:4-5 ; and a light chain variable region comprising a CDR1-3 of SEQ ID NO:7-9. Shelton et al also teaches nucleic acid encoding an agonist anti-trkC antibody, a vector, a host cell, a pharmaceutical composition and a kit. Shelton does not teach a method of interchanging the amino acid residues within the CDR regions, making an agonist anti-trkC antibody, said method comprising expressing a polynucleotide encoding the agonist anti-trkC antibody, in addition to a polypeptide that binds to trkC comprising the said CDRs and the said changes within the CDR. These deficiencies are made up for by Devaux et al and Segal et al.

Segal et al teach a target specific cross-linked heteroantibody (specifically mouse monoclonal antibody 2256, the antibody of the present study) and a method of producing the same, wherein heteroantibodies can cause normal autologous cells of the immune system to destroy any unwanted cell for which an antibody is available. Segal et al teach that the treatment or control of tumors, viral infected cells, fungi, bacteria, parasites and the like is now made possible through the use of the heteroantibody complex of the present invention.

Devaux et al teach agonist anti-trkC monoclonal antoibodies, in addition to the use of the use of the agonist antibodies in the prevention and/or treatment of cellular degeneration, including nerve cell damage associated with acute nervous cell system injury and chronic neurodegenerative diseases, including peripheral neuropathy.

Therefore, claims 1-25 lack an inventive step under PCT Article 33(3) as being obvious over Shelton et al (PGPUB 2005/0089521A1; Filed December 23, 2003, Claims priority to December 23rd, 2003) in view of Segal et al (U.S. Patent 4,676,980; Issue Date: June 30th, 1987), and further in view of Devaux et al (Filed October 30th, 2003)..